REMARKS

Reconsideration of the present application in view of the following remarks is respectfully requested. Claims 1-27 and 44-70 are pending; claims 1-27, 48-51 and 55-70 have been withdrawn and claims 52-54 are under consideration. By the present amendment, claim 54 has been canceled without prejudice and the specification has been amended to remove an objected-to internet website address. Claims 52 and 53 are presently amended, and new claims 71-81 have been added to more particularly point out and distinctly claim certain embodiments encompassed by applicants' invention. Support for the present amendments can be found in the application as originally filed, for instance, in the specification at, *e.g.,* paragraphs 0005, 0009-0011, 0020, 0029, 0052, 0054, 0065, 0069, 0075, 0100-0102, 0117, 0140-0142, 0165-0169, 0208-0213, 0216, 0217, 0231-0233, 0237, 0238, 0240, 0241, 0243, 0247, 0253 and 0271. No new matter has been added.

SPECIFICATION

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. According to the Examiner's suggestion, Applicants have deleted the embedded hyperlink located at page 18, paragraph 0262.

CLAIM REJECTIONS UNDER 35 USC § 112, SECOND PARAGRAPH

The PTO rejects claims 52, 53 and 54 under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Specifically, the Examiner is unclear with respect to the meanings of "functionally interfering" and "substantially homologous". The Examiner is also unclear regarding the meaning of "wherein the agent hybridized to the Domain III" in claim 54, asserting that such recitation lacks antecedent basis. The Examiner further requests clarification with respect to whether it is the agent or the domain III that has a sequence substantially homologous to SEQ ID NOS:20 and 21.

Applicants traverse these grounds for rejection. In presently claimed embodiments, the invention is directed in pertinent part to a method for controlling entry of a flavivirus into a cell, the flavivirus exhibiting a flavivirus envelope protein, the flavivirus

envelope protein comprising a domain III of the flavivirus envelope protein, the method comprising administering to the cell an agent that functionally interferes with binding of domain III of the flavivirus envelope protein to a flavivirus receptor protein, wherein the agent comprises a polypeptide having an amino acid sequence that exhibits at least 80% sequence similarity to amino acids 350 to 390 of a flavivirus envelope sequence as set forth in SEQ ID NO: 21, and wherein the flavivirus receptor protein is one of an integrin and a neurotensin receptor. Applicants submit that as amended herewith the present claims particularly point out and distinctly claim the subject matter which applicants regard as being encompassed by the invention, in full compliance with 35 U.S.C. §112, second paragraph.

As an initial note, by cancellation of claim 54 according to the amendment submitted herewith, the rejection of claim 54 is obviated and should therefore be withdrawn. Applicants also note that amended claim 53 no longer recites "substantially homologous", such that the rejection of claim 53 under 35 U.S.C. §112, second paragraph, has been rendered moot.

The test for indefiniteness is whether one of ordinary skill in the art would understand the bounds of the claim, when read in light of the specification and in the context of the prior art. Applicants respectfully submit that in view of the present amendments, which are made not in acquiescence to any rejection but instead solely to make explicit what was already implicit, the skilled person would readily understand what is meant by an agent that "functionally interferes" with *binding* of the domain III of the flavivirus envelope protein *to a flavivirus receptor protein.*

As disclosed in the present specification and recited in the instant claims, the presently claimed invention embodiments relate to applicants' discovery of the identities of cellular flavivirus receptor proteins, with which flavivirus envelope protein domain III interacts to effect flavivirus binding to host cells. The identities of such flavivirus receptor proteins were not known prior to the instant application (see, *e.g.*, specification at paragraphs 0005-0007). The present application thus for the first time teaches domain III-binding flavivirus receptor proteins, including, *inter alia*, integrins (*e.g.*, paragraphs 0068-0083, 0208-0213) and neurotensin receptor (*e.g.*, paragraphs 0094-0098, 0230-0233). The present application also discloses and claims a method for controlling entry of a flavivirus into a cell that relates to the use of a competitive

ligand, such as a peptide that is complementary to the flavivirus envelope protein domain III-binding region of an integrin or neurotensin receptor (*e.g.*, specification at paragraphs 0099-0102).

Accordingly, the instant specification discloses that the flavivirus envelope protein domain III functionally interacts, through its binding interactions, with a flavivirus receptor protein, wherein the flavivirus receptor protein is an integrin or a neurotensin receptor. The specification also teaches that when an agent *functionally interferes* with such a binding interaction includes a reference to altered (*i.e.*, enhanced or inhibited) functionality, *e.g.*, altered binding, in the presence of the agent compared to the functionality in the absence of the agent. For example, such an agent may interfere with functionality of the envelope protein molecule domain III, and/or of the flavivirus receptor protein molecule, by binding to the molecule, or by sterically hindering the binding interaction between the flavivirus envelope protein domain III and the flavivirus receptor protein, *see e.g.*, paragraph 0142. Such interference with binding of domain III to the flavivirus receptor protein may thereby influence flavivirus entry, for instance, by inhibiting domain III function through activity of the agent as a competitive ligand (*see e.g.*, paragraphs 0100-0102).

Applicants therefore submit that the specification makes abundantly clear what it means to functionally interfere with binding of the domain III of the flavivirus envelope protein to a flavivirus receptor protein, and thus respectfully request withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

CLAIM REJECTIONS UNDER 35 USC § 112, FIRST PARAGRAPH (WRITTEN DESCRIPTION)

The PTO rejects claims 52-54 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Office Action asserts that the specification has not provided sufficient examples or structural characteristics regarding an agent that functionally interferes with domain III of the flavivirus envelope protein to provide adequate support for the entire scope of the claimed genus.

Applicants respectfully traverse these grounds for rejection and submit that the specification supports the full scope of the claimed subject matter, and that the application therefore satisfies the requirements of 35 U.S.C. §112, first paragraph. As also noted above, the presently claimed embodiments are directed in pertinent part to a method for controlling entry of a flavivirus into a cell, wherein the flavivirus exhibits a flavivirus envelope protein that comprises a domain III, and wherein the method comprises administering to the cell an agent that functionally interferes with binding of the domain III to a flavivirus receptor protein, *wherein the agent comprises* a polypeptide having an amino acid sequence that exhibits at least 80% sequence similarity to amino acids 350 to 390 of a flavivirus envelope sequence as set forth in SEQ ID NO: 21, and wherein the flavivirus receptor protein is an integrin or a neurotensin receptor.

Applicants submit that the specification reasonably conveys to a skilled artisan that Applicants were in possession of the claimed invention at the time of filing by providing sufficient, detailed and relevant identifying characteristics of the recited agent. As disclosed in the specification and recited in the claims, an agent that functionally interferes with binding of the domain III of the flavivirus envelope protein to a flavivirus receptor protein comprises a polypeptide having a sequence that exhibits at least 80% sequence similarity to amino acids 350-390 of a flavivirus envelope sequence as set forth in SEQ ID NO:21. Support for functional characteristics that identify the recited agent are also discussed above, including specification support for determining when an agent is present that "functionally interferes with binding" *of* the flavivirus envelope protein domain III *to* a flavivirus receptor protein, and abundant structural characteristics of such an agent are also provided by the specification, as discussed herein.

For example, paragraphs 0099-0102 of the application summarize, and paragraphs 0237-0238 and 0240-0243 describe in great detail, the preparation and functional characterization of a soluble domain III polypeptide agent having amino acids 350-390 of SEQ ID NO:21, the West Nile Virus envelope protein sequence which contains domain III. As described in the specification, *e.g.*, in paragraphs 0240-0241, identification of the domain III portion of a flavivirus envelope protein (*i.e.*, a portion that includes amino acids 350-390 of SEQ

ID NO:21) is well known to a person skilled in the relevant art at the time of filing. That which is already well known in the art need not be described again in the specification. *Capon v. Eshhar*, 76 USPQ2d 1078, 1085 (Fed. Cir. 2005).

Additionally, the present specification, *e.g.*, at paragraph 0024, describes a method for controlling flavivirus entry into a cell by administering an agent that functionally interferes with a flavivirus envelope protein domain III, wherein the domain III comprises a sequence portion that is substantially homologous to SEQ ID NO:21. Paragraph 0065 and Fig. 23 depict just such a method, whereby the soluble domain III polypeptide of paragraphs 0240-0241 blocks entry of a flavivirus, West Nile Virus, into cells. In paragraph 0081, for example, the specification teaches that a functionally interfering agent may be a competitive ligand that interferes with integrin function, and paragraph 0083 teaches that such competitive ligands, which are peptides complementary to the binding region in the integrin, can be identified and manufactured by a skilled person based on the instant specification.

Paragraph 0086 teaches, for example, competitive ligands that include RGE-containing peptides, where it is noted that SEQ ID NO:21 has the sequence RGE at amino acid positions 389-390, which are within the recited region of amino acids 350 to 390. At paragraphs 0198-0205 and 0208-0213, the specification discloses detailed experimental results showing that flavivirus binding to cells, leading to viral infection, is an integrin-mediated function. Similarly with respect to an agent that functionally interferes with binding of the flavivirus envelope protein domain III to a neurotensin receptor, the specification, *e.g.*, at paragraphs 0097-0098, describes synthetic peptides that are competitive ligands complementary to the neurotensin receptor binding region for neurotension. At, *e.g.*, paragraphs 0229-0233 and 0062, and Figure 20, the specification teaches neurotensin receptor cDNA isolation and expression in a host cell, and a screening assay for flavivirus binding inhibitors by detecting agents that are capable of blocking West Nile Virus entry into neurotensin-receptor-transfected cells.

The specification at, *e.g.*, paragraphs 0102 and 0117, discloses that the agent can be a peptide that is complementary to the binding region for domain III (see, *e.g.*, paragraphs 0098-0101) in the integrin, or in the neurotensin receptor (see, *e.g.*, paragraphs 0095 and 0097). At paragraphs 0140-0141, for example, the specification teaches further that polypeptides

described in the instant application may be modified, including "deliberate or accidental modifications of the original sequence, such as deletions, additions and substitutions, so long as the desired activity is maintained".

Moreover, the specification teaches (*e.g.*, paragraph 0141) that a polypeptide may exhibit at least 80-85%, 90% or 95-98% sequence similarity, or may be completely identical, to a specified sequence, where Applicants submit that the design and synthesis of a polypeptide having a desired amino acid sequence was well within the state of the art at the time of filing the instant application. As also noted above, that which is already well known in the art need not be described again in the specification. *Capon v. Eshhar*, 76 USPQ2d 1078, 1085 (Fed. Cir. 2005). Hence, the specification clearly evidences Applicants' possession of a peptide having the recited functional (*e.g.*, interferes with domain III binding) and structural (*e.g.*, at least 80% sequence similarity to domain III amino acids 350-390) characteristics.

Accordingly, Applicants submit that the specification provides sufficient, detailed and relevant identifying characteristics of the presently recited agent comprising a polypeptide having a sequence that exhibits at least 80% sequence similarity to amino acids 350 to 390 of a flavivirus envelope sequence as set forth in SEQ ID NO:21 (*e.g.*, a sequence as disclosed in paragraphs 0240-0241). The instant claims therefore satisfy the written description requirements of 35 U.S.C. §112, first paragraph, such that withdrawal of the rejection is respectfully requested.

CLAIM REJECTIONS UNDER 35 USC § 112, FIRST PARAGRAPH (ENABLEMENT)

The PTO rejects claims 52 and 53 under 35 U.S.C. §112, first paragraph, alleging that the subject matter of these claims is not enabled by the specification. In particular, the Office Action concedes that the specification is enabling for a specific portion of flavivirus envelope protein domain III, but asserts that undue experimentation would be required to practice the claimed invention with respect to the entire domain III sequence.

Applicants respectfully traverse these grounds for rejection and submit that all requirements of 35 U.S.C. §112, first paragraph, are satisfied by the present application. As also discussed above, the presently claimed invention embodiments are directed in pertinent part to a method for controlling entry of a flavivirus into a cell, comprising administering to the cell an

agent that functionally interferes with binding of the flavivirus envelope protein domain III to a flavivirus receptor protein, wherein the agent comprises a polypeptide having an amino acid sequence that exhibits at least 80% sequence similarity to amino acids 350 to 390 of a flavivirus envelope sequence as set forth in SEQ ID NO: 21. For reasons also given above, Applicants submit the specification provides abundant guidance in a manner that would enable a skilled person to practice the claimed method readily and without undue experimentation.

For enablement purposes, adequate support for generic claims to biological subject matter "depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations . . .". *Capon v. Eshhar*, 76 USPQ2d 1078, 1085 (Fed. Cir. 2005). With regard to the state of the art, the assertion in the Office Action, that Beasley et al. teach interference with domain III epitopes resulting in virus neutralization, is beside the point. Beasley et al. fail to recognize that structurally distinct flavivirus envelope protein domains III, whether from West Nile Virus, Dengue virus or Japanese Encephalitis Virus, bind to a flavivirus receptor protein such as an integrin or a neurotensin receptor. At the time of filing the instant application, the state of the art thus failed to appreciate that an agent as recited in the instant claims interferes with domain III binding to a flavivirus receptor protein (*e.g.*, integrin or neurotensin receptor). As such, the art could not routinely identify an agent as presently recited because the target flavivirus receptor protein was unknown. The state of the art instead believed that distinct antibodies reactive with the structurally distinct flavivirus envelope protein domains III would be needed.

Applicants respectfully submit that, in particular, the *Wands* analysis found at pages 8-10 of the outstanding Office Action is inapposite in view of the instant claims recitations, the disclosure in the instant specification and the state of the art at the time of filing. Undue experimentation would not be required where the person skilled in the art would, given the instant specification, clearly know how to identify and/or obtain a polypeptide having at least 80% amino acid sequence identity to the recited portion (amino acids 350 to 390 of SEQ ID NO:21) of the flavivirus envelope protein domain III (see, *e.g.*, Sequence Listing, and specification at paragraphs 0240-0241, and 0140-0141).

The specification clearly teaches how to determine that the recited polypeptide interferes with flavivirus binding to a flavivirus receptor protein, such as an integrin or a neurotensin receptor, via envelope protein domain III (*e.g.*, specification at paragraphs 0231-0246). Furthermore, based on the discovery disclosed for the first time in the present application that, *inter alia*, integrins and neurotension receptors are flavivirus receptor proteins, Applicants note that the specification describes functional *interference with* binding to such flavivirus receptor proteins (*i.e.*, integrins or neurotensin receptors) by envelope protein domain III sequences from flaviviridae of different subgroups, *e.g.*, domain III sequences from West Nile Virus and Dengue Virus, (*e.g.*, paragraph 0065), as well as domain III sequences from Japanese Encephalitis Virus, (*e.g.*, paragraph 0054). These working examples represent flaviviruses having domain III polypeptides that vary in their amino acid sequences by up to 45%, (*see e.g.*, NCBI sequence identity comparison, enclosed for the Examiner's convenience). Control of cellular entry by these flaviviruses, however, can still be achieved according to the claimed methods, where the present application demonstrates susceptibility of each flavivirus to interference with receptor-binding, based on the unexpected discovery that integrins and neurotensin receptors function as flavivirus receptor proteins. Accordingly, the recited polypeptide agent is thus provided, which as a functionally interfering competitive ligand, is complementary to the domain III-binding region *of such an integrin or neurotensin receptor flavivirus receptor protein* (*e.g.*, specification at paragraph 0117), to control viral entry into a cell.

Applicants therefore submit that, contrary to the assertions found in the Office Action, the breadth of the instant claims is commensurate with the scope of the disclosure, in view of the presence of working examples (*e.g.*, Figs. 11-12, Example 14; Fig. 23, Example 22), the state of the prior art (discussed above), the relative skill of those in the art (typically very high, given the educational background and sophistication common in the biotechnology arts), and the guidance provided in the specification (also discussed above). Even under *Wands*, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification . . . provides a reasonable amount of guidance with respect to the direction in which

the experimentation should proceed." *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

In view of the foregoing, Applicants respectfully submit that the application satisfies all requirements under 35 U.S.C. §112, first paragraph, and request that the rejections be withdrawn.

CLAIM REJECTIONS UNDER 35 USC §102

The PTO rejects claim 52 under 35 U.S.C. §102(b) as being allegedly anticipated by Crill et al. (2001 *Journal of Virology*, 75(16):4469-73). Specifically, the Office Action asserts that Crill et al. teach a monoclonal antibody that binds to domain III of a flavivirus, which blocks or interferes with virus adsorption to cells.

Applicants respectfully traverse this rejection and submit that Crill et al. fail to anticipate the subject matter of claim 52. According to the embodiments encompassed by claim 52 as amended herewith, the present invention is directed in pertinent part to a method for controlling entry of a flavivirus into a cell, the method comprising administering to the cell an agent that functionally interferes with the binding of domain III of the flavivirus envelope protein to a flavivirus receptor protein, wherein the agent comprises a polypeptide having a sequence that exhibits at least 80% sequence similarity to amino acids 350 to 390 of a flavivirus envelope sequence as set forth in SEQ ID NO: 21, wherein the flavivirus receptor protein is one of an integrin and a neurotensin receptor.

It is axiomatic that in order for the PTO to establish a *prima facie* case of anticipation, it must show that each and every element of the claim is disclosed within the cited reference. Applicant submits that the teachings of Crill et al. are limited to monoclonal antibodies directed against Dengue Virus type 2 α-domain III. Crill et al. fail, however, to teach or suggest any other agent capable of functionally interfering with domain III of a flavivirus, such as the polypeptide agent having at least 80% sequence similarity to amino acids 350 to 390 of SEQ ID NO:21, according to the instant claim. In addition, Crill et al. fail to teach or suggest that the flavivirus receptor protein is an integrin or a neurotensin receptor.

Accordingly, the PTO has not established a case of *prima facie* anticipation by Crill et al., where Crill et al. fail to disclose each and every element of the instant claim. Withdrawal of the rejection under §102(b) is respectfully requested.

CLAIM REJECTIONS UNDER 35 USC § 103

Claim 53 stands rejected under 35 U.S.C. §103(a) for alleged obviousness over Crill et al. (2001 *Journal of Virology*, 75(16):4469-73) in view of Beasley et al. (2002 *Journal of Virology,* 76(24):13097-13100). Specifically, the Examiner concedes that Crill et al. do not teach the claimed method wherein the domain III sequence has a sequence substantially homologous to SEQ ID NO: 21. The Office Action asserts, however, that Crill et al. teach that domain III encodes the primary flavivirus receptor binding motif, and that Crill et al. also disclose monoclonal antibodies that functionally interfere with domain III. The Action asserts further that Beasley et al. teach neutralizing epitopes within domain III that contain variable homology to SEQ ID NO: 21. According to the Examiner, the skilled artisan would have been motivated to combine the teachings of Crill et al. and Beasley et al. to arrive at the claimed method wherein the flavivirus exhibits an envelope protein comprising a domain III that is substantially homologous to SEQ ID NO:21.

Claim 54 stands rejected under 35 U.S.C. §103(a) for alleged obviousness over Crill et al. and Beasley et al., in view of Wu et al. (2001 *Virus Researc*h 76:59-69). Crill et al. and Beasley et al. are described above, and the PTO concedes that these references fail to teach the claimed method wherein the agent hybridized to domain III has a sequence substantially homologous to SEQ ID NO: 21. The Office Action asserts, however, that Wu et al. teach peptide ligands that mimic the conformational epitopes on domain III of a flavivirus, and that said epitopes elicit α-domain III neutralizing antibodies. Applicants note that claim 54 has been canceled without prejudice by amendment herewith, thereby rendering moot the rejection of that claim.

Applicants traverse these grounds for rejection and submit that the presently claimed subject matter is non-obvious. In particular, the prior art fails to teach or suggest a method for controlling flavivirus entry into a cell using an agent that interferes with binding of a

flavivirus envelope protein domain III to an integrin or a neurotensin receptor, because prior to the present application, the art was not aware that an integrin or a neurotensin receptor can function as a flavivirus receptor protein. In addition, the prior art fails to teach or suggest the use in such a method of an agent comprising a polypeptide having a sequence that exhibits at least 80% sequence similarity to amino acids 350 to 390 of the flavivirus envelope sequence set forth in SEQ ID NO:21. Applicants submit that it would be impermissible hindsight in view of the instant application to allege that the prior art in any way suggested the presently claimed embodiments, particularly where only from the application would a person having ordinary skill in the art reasonably expect successfully to generate an agent having the recited polypeptide structure and being capable of interfering with domain III binding to a flavivirus receptor protein.

The cited references, individually or combined, fail to teach or in any way suggest the subject matter of the present claims as amended herewith. Thus, the PTO has failed to establish a *prima facie* case of obviousness under 35 USC §103(a). (*See In re Mayne*, 104 F.3d 133, 1341-43, 41 U.S.P.Q.2d 1451 (Fed. Cir. 1997) (PTO has the burden of showing a *prima facie* case of obviousness.)). The PTO must show (1) that the cited reference(s) teaches or suggests all claim elements; (2) that the reference provides some teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce the claimed invention; and (3) that according to the teachings of the reference, a person having ordinary skill in the art will achieve the claimed invention with a reasonable expectation of success. When rejection of claims depends upon a combination of prior art references, a teaching, motivation, or suggestion to combine the references must exist. (*See In re Rouffet*, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998)).

Applicants note that the agent as recited for use in the claimed method comprises a polypeptide having a sequence that exhibits at least 80% sequence similarity to amino acids 350 to 390 of the flavivirus envelope protein sequence set forth in SEQ ID NO:21. Crill et al. and Beasley et al., by contrast, fail even remotely to contemplate such an agent, but are instead limited in their teachings to the use of anti-domain III monoclonal antibodies. The PTO fails to establish a case of *prima facie* obviousness where there is no evidence that any of the anti-

domain III antibodies described in the cited documents necessarily exhibit at least 80% sequence similarity to amino acids 350 to 390 of the flavivirus envelope protein sequence set forth in SEQ ID NO:21, nor has the PTO pointed to any suggestion in the cited references to use the teachings found therein to arrive at the presently claimed subject matter.

Wu et al. fail to remedy the deficiencies of Crill et al. and Beasley et al. Wu et al. fail to teach or suggest a method for controlling flavivirus entry into a cell comprising administering an agent that functionally interferes with flavivirus envelope protein domain III binding to an integrin or a neurotensin receptor, wherein the agent comprises a polypeptide having a sequence exhibiting 80% sequence similarity to amino acids 350 to 390 of SEQ ID NO:21.

Wu et al. merely teach peptides that elicit an anti-domain III neutralizing antibody response, in contrast to the agent recited in the claims of the present application, which relates to peptides that functionally interfere with domain III binding to a flavivirus receptor. In addition, and contrary to the assertion found in the Office Action that the person of ordinary skill would have been motivated to combine Wu et al. with the other cited documents, Wu et al. teach away from the presently claimed methods. For example, the peptides in Wu et al. restored flaviviral infectivity in the presence of otherwise neutralizing antibodies. As described by Wu et al. at pages 64-65 and in Fig. 3 (page 66), the polypeptides of Wu et al. did not inhibit flavivirus entry into a cell and did not interfere with flavivirus binding to a flavivirus receptor, but instead occupied neutralizing antibody binding sites, thereby facilitating infection of cells by flavivirus (JEV). In marked contrast, the domain III-like polypeptide agent of the present claims directly inhibits flaviviral infectivity by functionally interfering with domain III binding to the flavivirus receptor.

Moreover, the domain III peptide mimetics described by Wu et al. are characterized by a predicted three-dimensional structural similarity to domain III of JEV E protein, but the peptides of Wu et al. exhibit no sequence similarity to amino acids 350 to 390 of the domain III sequence set forth in SEQ ID NO: 21. As such, a person having ordinary skill in the art, given Crill et al., Beasley et al. and Wu et al., would not have been motivated, with the requisite reasonable expectation of success, to arrive at the presently claimed subject matter.

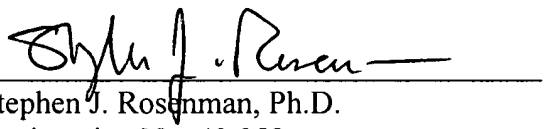
Accordingly and for the foregoing reasons, Applicants submit that the PTO has established no *prima facie* case of obviousness, such that withdrawal of the rejections under 35 U.S.C. §103 is respectfully requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



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SJR:rp

Enclosures:
Dengue Virus, West Nile Virus and Japanese Encephalitis Virus Domain III Sequence Comparisons (6 pages)

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